FORMULAITE

Simulaite Report

Cannabinoid Nanoemulsion Pharmacokinetics

Capsoil 2025 clinical benchmark vs Formulaite PBPK simulation

June 25, 2026

Executive Summary

Formulaite simulated the same THC/CBD self-emulsified powder used in Hermush et al. (J Cannabis Res 7, 35 (2025)) and compared it to a tincture control matched to the study design. Reported PK metrics — bioavailability, Cmax, Tmax, AUC, and plasma concentration–time profiles — come directly from the Simulaite PBPK engine output for each virtual subject and are summarized across the cohort.

Validation Takeaway

Ratios below compare the nano powder arm to the tincture control in the same virtual cohort.

- THC: nano/control AUC ratio Simulaite 2.28× vs paper 2.86×; Simulaite Cmax ratio 2.49×.
- CBD: nano/control AUC ratio Simulaite 2.26× vs paper 2.27×; Simulaite Cmax ratio 2.73×.
- The model captures the key clinical direction: nano powder is faster and gives roughly doubled AUC versus tincture control.

Molecules

Name	SMILES
THC	CCCCCC1=CC(=C2[C@@H]3C=C(CC[C@H]3C(OC2=C1)(C)C)C)O
CBD	CCCCCC1=CC(=C(C(=C1)O)[C@@H]2C=C(CC[C@H]2C(=C)C)C)O

We use our suite of graph neural networks to predict relevant molecular properties and interactions with liver enzymes, plasma proteins, and the gut wall to inform the simulations.

Formulations

1. Tincture control

Formulation type	Oil tincture (MCT vehicle)
Active dose	8 mg THC + 8 mg CBD
Vehicle oil	80 mg medium-chain triglyceride oil
Administration	Short sublingual hold, remainder swallowed; fasted state

Ingredient	Amount
Delta-9-tetrahydrocannabinol (THC)	8.0 mg
Cannabidiol (CBD)	8.0 mg

Ingredient	Amount
Medium-chain triglyceride (MCT) oil	80.0 mg

2. Capsoil self-emulsified nano powder

Formulation type	Self-nanoemulsifying powder (oral)
Active dose	8 mg THC + 8 mg CBD per dose (matches Hermush et al. 2025)
Post-redispersion D50	158.0 nm after powder re-dispersion
In-use dilution	250 mL total (125 mL reconstitution + 125 mL rinse)
Administration	Powder redispersed in water, oral absorption; fasted state

Delta-9-tetrahydrocannabinol (THC)	8.0 mg
Cannabidiol (CBD)	8.0 mg
Olive oil (lipid phase)	45.0 mg
Polysorbate 80 (Tween 80)	80.0 mg
Post-redispersion D50	158.0 nm
Reconstitution volume	250 mL

What happens after the powder is mixed

In the clinic, the powder is mixed with water before swallowing (125 mL reconstitution + 125 mL rinse in Hermush et al.). That forms a fine oil-in-water emulsion after re-dispersion (about 158.0 nm in the Hermush study) - the in-use product we model, not the dry powder on its own.

- Droplet-size modeling: measured post-redispersion droplet size sets oil-water contact area; finer emulsions expose more surface and release cannabinoids from the oil phase sooner.
- Colloidal partitioning: after reconstitution, the dose is split prospectively across immediately available gut fluid, surfactant-stabilized colloid, and oil droplets, based on the product recipe and droplet size - not tuned to match the clinical curves.
- Lipolysis: in the upper small intestine, we apply published lipid-digestion behavior (lipase and bile breaking down triglyceride droplets) to release drug from the oil core over time.
- Solubilization and uptake: released cannabinoids partition between oil remnant, surfactant assemblies, and aqueous phase at the intestinal wall; lipophilic actives may also use lymphatic routes alongside digested lipids.

Population Settings

Population	American (with Census Demographics)
Population Type	American mixed proportional
Sample Size (n)	100
Age Range	19–65 years (mean 43)
Female %	49%
Weight	47–135 kg (mean 79 kg)
Height	141–191 cm (mean 169 cm)
BMI	19–50 kg/m² (mean 28)
Race/Ethnicity	White 62% · Latino 19% · African American 13% · Asian 6%
Prandial State	Fasted
Simulation Duration	24 h

The same virtual cohort was simulated independently under each formulation arm; differences reflect formulation modeling rather than subject composition.

PK Results

Arm	Compound	F	Cmax	Tmax	AUC0-24
Tincture control	**THC**	1.64%	6.64 ng/mL	7.20 h	116.43 ng·h/mL
Tincture control	**CBD**	2.32%	7.44 ng/mL	10.20 h	135.22 ng·h/mL
Nano powder	**THC**	3.65%	16.52 ng/mL	2.88 h	265.47 ng·h/mL
Nano powder	**CBD**	5.09%	20.33 ng/mL	3.96 h	305.85 ng·h/mL

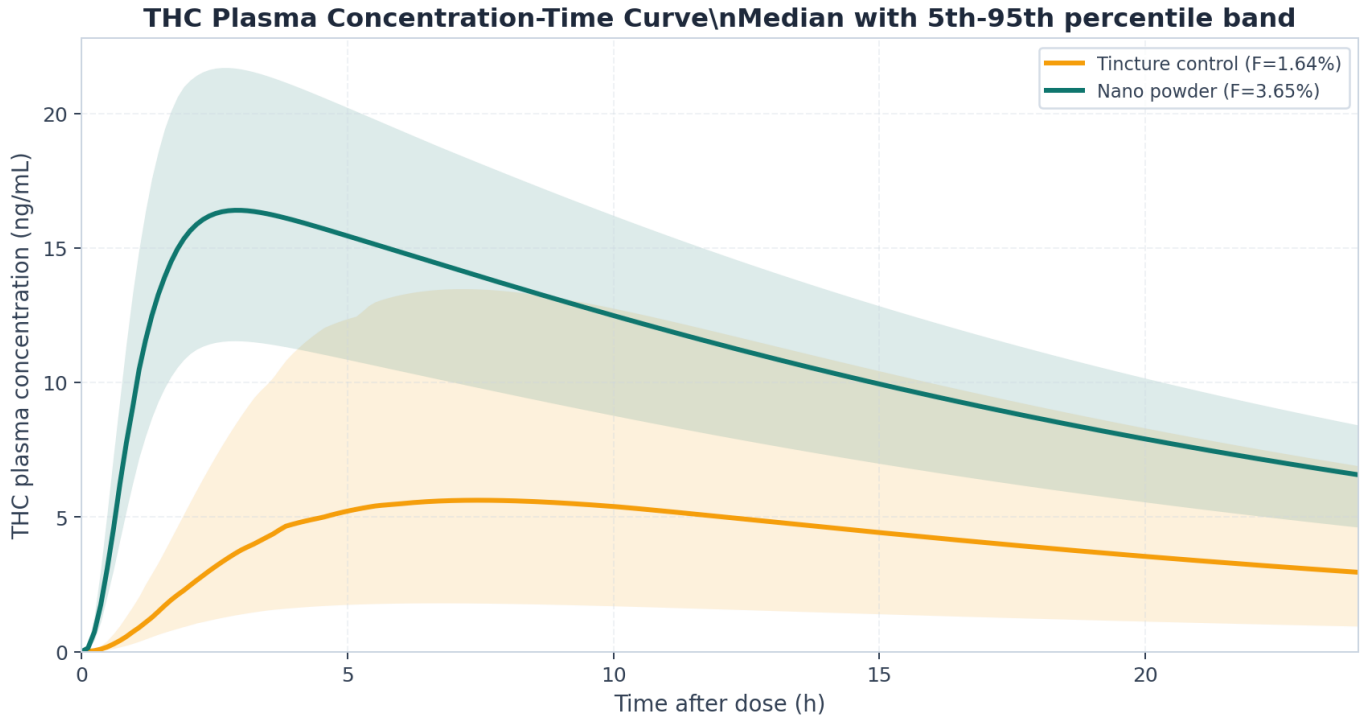
Clinical Relative Bioavailability Comparison

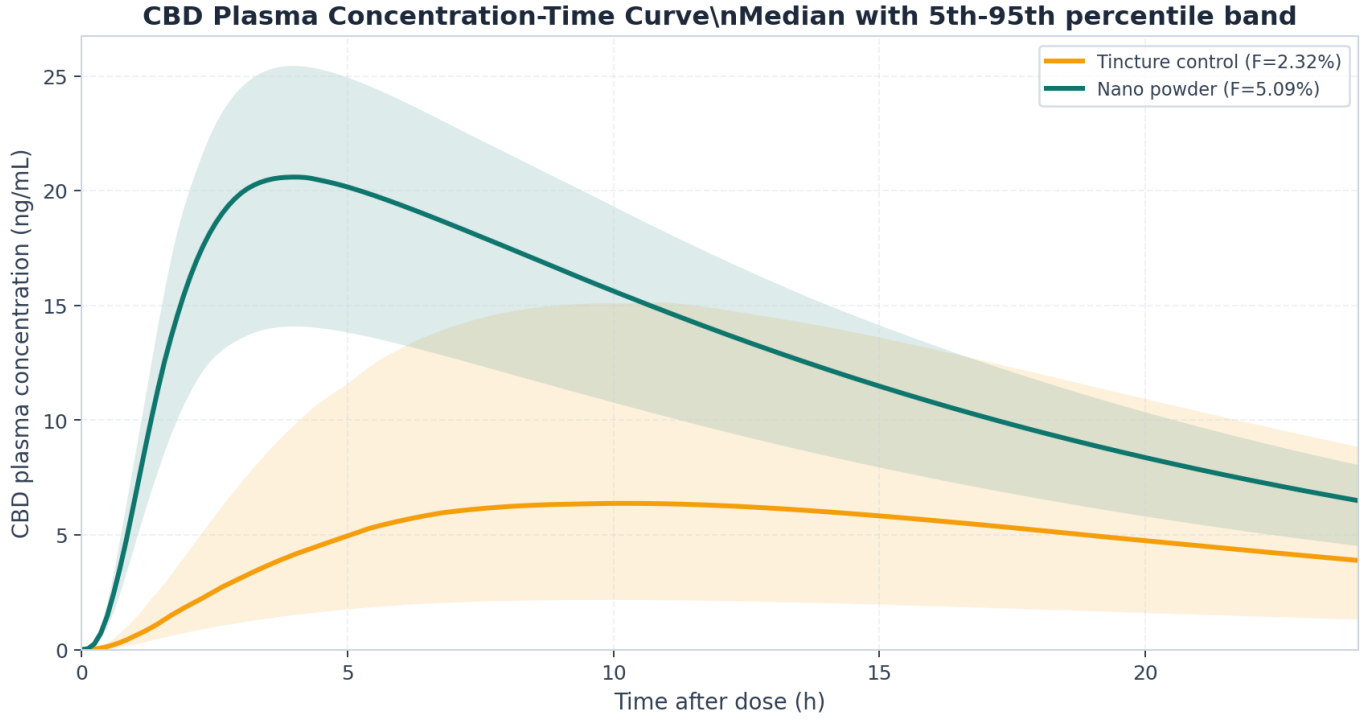
Hermush et al. (J Cannabis Res 7, 35 (2025)) reports the nano powder as 100% relative bioavailability, with the tincture control at 35% for THC and 44% for CBD. Therefore the clinical nano/control AUC ratios are 2.86× for THC and 2.27× for CBD.

Compound	Paper oil relative BA	Paper nano/control AUC	Simulaite nano/control AUC0-24	Delta
THC	35%	2.86×	**2.28×**	-20.2%
CBD	44%	2.27×	**2.26×**	-0.5%

Plasma Concentration Curves

These plots are generated from formatter-backed production pk_profiles, using stored molecular-weight metadata for umol/L to ng/mL conversion.





Advanced Details (Predicted)

Enzyme contributions, P-gp substrate probability, and inhibition flags are ADMET model predictions — not clinically validated values.

Metabolic Clearance — Enzyme Contributions

Compound	CYP1A2	CYP3A4	CYP2D6	CYP2C9	CYP2C19	UGT1A1	SULT1A1	P-gp sub.
THC	—	29.6%	18.8%	10.2%	—	**41.3% ***	—	Yes

Compound	CYP1A2	CYP3A4	CYP2D6	CYP2C9	CYP2C19	UGT1A1	SULT1A1	P-gp sub.
CBD	—	28.3%	18.8%	11.5%	—	**41.4% ***	—	Yes

Enzyme Inhibition Profile

Compound	CYP1A2	CYP3A4	CYP2D6	CYP2C9	CYP2C19	UGT1A1	SULT1A1	P-gp inh.
THC	**Yes**	**Yes**	—	**Yes**	**Yes**	—	—	**Yes**
CBD	—	**Yes**	—	**Yes**	—	—	—	**Yes**

Inhibition probability >=50% = inhibitor. Relevant for co-administration with CYP substrates.

Clinical benchmark reference: Vered Hermush, Nisim Mizrahi, Tal Brodezky, and Rafael Ezra. Enhancing cannabinoid bioavailability: a crossover study comparing a novel self-nanoemulsifying drug delivery system and a commercial oil-based formulation. J Cannabis Res 7, 35 (2025). DOI: 10.1186/s42238-025-00294-8. https://pmc.ncbi.nlm.nih.gov/articles/PMC12166629/

Pharmacokinetic Simulation Methodology

Simulaite Pharmacokinetics is a fully in silico physiologically based pharmacokinetic (PBPK) engine that predicts bioavailability directly from product specifications. ADMET properties are predicted using an ensemble of in-house graph neural networks trained on curated molecular, physicochemical, and bioactivity datasets. These predictions feed into a full compartmental PBPK framework taking into account lymphatic transport, transmucosal absorption, excipient-aware formulation modeling, and multi-compound interactions. Population variability is represented using published demographically matched physiological statistics, enabling matched virtual cohort analysis.

For formulation comparisons, the same virtual cohort is simulated independently under each formulation, so differences reflect modeled formulation assumptions rather than differences in subject composition.

Selected Public PK Methodology References

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